**AMENDMENT**

In the Specification:

Following the abstract, please insert the enclosed Substitute Sheets as replacement pages 1 through 3 of the Sequence Listing submitted on November 13, 2001.

Please enter the following replacement paragraphs:

**[0058]** In one embodiment the TGF-α polypeptide, related polypeptide, mimetic or functional fragment is a TGF-α polypeptide as set forth in SEQ ID NO:1, SEQ ID NO:3, or a TGFα mimetic selected from the group consisting of formula I, formula II, formula III, formula IV, or formula V, wherein formula I is:

$R_1$- T - $R_2$ (I)

wherein $R_1$ is -$NH_2$, or $R_1$ is $R_3$ - $X_3$ , wherein $R_3$ is a polyethylene glycol (PEG) attached to the free $NH_2$ moiety of $X_3$ (wherein $X_3$ is Lys or Asp) and having a molecular weight of PEG of from about 2000 daltons to about 10,000 daltons, or one or more of the following seven amino acids from formula IV, including either L (natural) or D chiral orientations:

-$NH_2$-$X_{1a}$ -$X_{1a}$- Ser - His - Phe - Asn - $X_3$- (SEQ ID NO: 7) (IV)

wherein $X_{1a}$ is independently Val, Gly or Ala and $X_3$ is Lys or Asp;

wherein T is the native sequence of human TGFα (SEQ ID NO. 1) from amino acid residue no. 8 (Cys) to amino acid residue no. 43 (Cys) consisting of native L amino acids; and

wherein $R_2$ is -COOH or one of more of the following seven amino acids, including either L (natural) or D chiral orientations, from formula V:

-$X_4$- His - $X_{1c}$- $X_4$- $X_5$- $X_6$- $X_{1c}$- (SEQ ID NO: 5) (V)

wherein $X_4$ is Glu or Asp, wherein $X_5$ is Leu or Ile, wherein $X_6$ is Asp or Glu, and wherein $X_{1c}$ is independently Val, Gly, or Ala.

**[0059]** The invention provides a peptide having TGF-α biological activity, comprising at least an 11-membered peptide compound of formula II:

-$NH_2$- $X_{1a}$-Cys-His-Ser-$X_{1b}$-$X_2$-$X_{1a}$-$X_{1b}$-$X_{1a}$-$X_3$-Cys COOH (SEQ ID NO:4) (II)

wherein $X_{1a}$, and $X_{1b}$ are independently Val, Gly, or Ala, wherein $X_2$ is Tyr or Phe, wherein $X_3$ is Arg or Lys, and wherein the two Cys moieties form a disulfide bond to create an 11-amino-acid functional peptide having a 10 member loop structure. In addition, at least one or more of the following amino acids of formula III may be added to the C terminus Cys moiety of formula II:

$$- X_4 - His - X_{1c} - X_4 - X_5 - X_6 - X_{1c} \text{ (SEQ ID NO: 5) (III)}$$

wherein $X_4$ is Glu or Asp, wherein $X_5$ is Leu or Ile, wherein $X_6$ is Asp or Glu and wherein $X_{1c}$ is Val, Gly or Ala. Preferably, $X_{1a}$ is Val, $X_{1b}$ is Gly and $X_{1c}$ is Ala thereby producing an 11, 12, 13, 14, 15, 16, 17 or 18 amino acid peptide. Preferably, $X_2$ is Tyr, and $X_3$ is Arg. Accordingly, in one embodiment the functional peptide of the invention has a sequence: $NH_2$-$X_{1a}$-Cys-His-Ser-$X_{1b}$-$X_2$-$X_{1a}$-$X_{1b}$-$X_{1a}$-$X_3$–Cys-$X_4$-His-$X_{1c}$-$X_4$-$X_5$-$X_6$-$X_{1c}$–COOH (SEQ ID NO:6)

**[0060]** SEQ ID NO: 6 forms a 10 member loop structure with a 7 member tail that can be varied in length. In addition, SEQ ID NO: 6 can form dimmers comprising, for example, a 34-mer peptide. Accordingly, the functional peptide can be from about 10 to 18 amino acids in length (*e.g.* 10, 11, 12, 13, 14, 15, 16, 17, or 18 amino acids) wherein $X_{1a}$ is Val, $X_{1b}$ is Gly, $X_{1c}$ is Ala and $X_4$ is Glu and may also comprise hetero- or homo-dimers of various TGF-α peptides described herein. Such dimers may have greater or reduced activities as compared to monomers.

**[0061]** The invention further provides an active TGF-α57 polypeptide (SEQ ID NO:3), wherein TGF-α57 is a 57 amino acid polypeptide having the formula VI:

Ser - Leu – Ser – Leu – Pro – Ala – Met – Human TGFα (SEQ ID NO: 3)
(VI)

Wherein human TGFα is a 50 amino acid polypeptide having a sequence as set forth in SEQ ID NO:1.

Please enter the following replacement paragraphs:

**[0151]** The invention further provides a bifunctional compound that acts as a TGFα mimetic, comprising a compound of formula III:

Loop peptide N-terminus-linker-cyclic $C_4H_8N_2$- linker- Loop peptide N-terminus

(VII)

Wherein the linker moiety is designed to link the N-terminus of the Loop peptide to a nitrogen atom of the ring $C_4H_8N_2$ and wherein the "loop peptide" comprises at least an 11-membered peptide compound of formula II:

$NH_2$- $X_{1a}$-Cys-His-Ser-$X_{1b}$-$X_2$-$X_{1a}$-$X_{1b}$-$X_{1a}$-$X_3$-Cys COOH (SEQ ID NO:4) (II)

wherein $X_{1a}$, and $X_{1b}$ are independently Val, Gly, or Ala; $X_2$ is Tyr or Phe; $X_3$ is Arg or Lys; and the two Cys moieties are linked via a disulfide bond to form an at least 11-amino acid functional peptide having TGF-α activity. Preferably, at least one or more of the following amino acids are added to the C terminus Cys moiety from formula III, below:

- $X_4$ - His - $X_{1c}$ - $X_4$ - $X_5$ - $X_6$ - $X_{1c}$ (SEQ ID NO: 5) (III)

wherein $X_4$ is Glu or Asp, wherein $X_5$ is Leu or Ile, wherein $X_6$ is Asp or Glu and wherein $X_{1c}$ is Val, Gly or Ala. Preferably, $X_{1a}$ is Val, $X_{1b}$ is Gly and $X_{1c}$ is Ala. Preferably the linker group is independently selected from the group consisting of substituted or unsubstituted $C_{1-6}$ alkoxy, xylenyl, wherein the substitutions are selected from the group consisting of: oxo, epoxyl, hydroxyl, chloryl, bromyl, fluoryl, and amino. Preferably, $X_2$ is Tyr, and $X_3$ is Arg. Most preferably, the functional peptide is 18 amino acids in length wherein $X_{1a}$ is Val, $X_{1b}$ is Gly, $X_{1c}$ is Ala and $X_4$ is Glu.

The invention will now be described in greater detail by reference to the following non-limiting examples.